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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,278	09/29/2003	David M. Goldenberg	329849	8186

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
06/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,278	GOLDENBERG ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8,9,14-16,29,31,32,34-37,39 and 48-107* is/are pending in the application.

4a) Of the above claim(s) *53-76 and 79-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,8,9,14-16,29,31,32,34-37,39,48-52,77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 4-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48, 49, and 77 have been amended.

Claim 3 has been cancelled.

Claims 53-76 and 79-107 remain withdrawn.

2. Claims 1, 4-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78 are under examination.

3. The following office action contains NEW GROUNDS of Rejection.

Objections Withdrawn

4. The objections to the specification are withdrawn in view of applicant's amendments to the specification.

Rejections Withdrawn

5. The rejection of claims 1, 3-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment to the claims.

6. The rejection of claims 1, 3-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, 48-52, 77, and 78 under 35 U.S.C. 103(a) as being obvious over Goldenberg, et al. as evidenced by Hansen, et al. and Becker, et al. in view of Hansen, et al. is withdrawn in view of applicant's declaration of common ownership.

7. The rejection of claims 1, 3-6, 8, 9, 14-16, 29, 31, 34-37, 39, and 48-52 under 35 U.S.C. 103(a) as being obvious over Goldenberg, et al. as evidenced by Hansen, et al. and Becker, et al. in view of Orlandi, et al., Cabilly, et al., Boss, et al., Robinson, et al. Ward, et al. and Huston, et al. is withdrawn in view of applicant's declaration of common ownership.

NEW GROUNDS of Rejection

Claim Objections

8. Claim 9 is objected to because of the following informalities: the claim contains a typographical error. Appropriate correction is required.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

> applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. The rejection of claims 1, 3-6, 8, 9, 14-16, 29, 31, 34-37, 39, and 48-52 under 35 U.S.C. 102(a, e) as being anticipated by Goldenberg, et al. as evidenced by Hansen, et al. and Becker, et al. is maintained.

Applicant's declaration filed January 18, 2008 has been carefully considered by the examiner but is deemed not to be persuasive. The declaration states that the hybridoma producing the MN3 antibody was not available to the public as of the filing date of the instant application. The declaration does not state that the hybridoma was never given out, only that it was not available "as of the filing date of the instant application of September 30, 2002". The declaration does not establish that the hybridoma was never given out at the time of the 102(a) date of February 21, 2002 or the 102(e) date of August 8, 2001, or at any time between the 1993 Hansen publication and the filing of the Goldenberg patent.

Therefore, after a fresh consideration of the claims and the evidence provided, the rejection is maintained.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 4-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, and 48-52 rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen, et al. (Cancer, 1993. Vol. 71, pages 3478-3485, as cited in the previous office action) as evidenced by the specification, in view of Robinson, et al. (US PAT 5,618,920 issued April 1994, as cited in the previous office action).

The claims recite a chimeric or humanized MN-3antibody or fragment thereof that binds NCA90 comprising the MN-3 light chain CDR sequences CDR1 (RSSQSIVHSNGNTYLE, SEQ ID NO: 1), CDR2 (KVSNRFS, SEQ ID NO:2) and CDR3 (FQGSHVPPT, SEQ ID NO:3) and the MN-3 heavy chain CDR sequences CDR1 (NYGMN, SEQ ID NO:4), CDR2 (WINTYTGEPTYADDFKG, SEQ ID NO:5) and CDR3 (KGWMDFNSSLDY, SEQ ID NO:6). The humanized antibody or fragment thereof of claim 1, wherein the antibody or fragment comprises the framework (FR) region sequences of the light and heavy chain variable regions of a human antibody and at least one light and heavy chain constant regions of a human antibody, wherein at least one of the FRs of the light and heavy chain variable regions of the humanized MN-3 antibody or fragment thereof comprises at least one amino acid substituted with the corresponding amino acid of the murine MN-3 antibody, wherein the at least one amino acid from the murine MN3 antibody is selected from the group consisting of amino acid residue 27, 30, 67, 68, 69 and 94 of the murine MN-3 heavy chain variable region sequence or amino acid residue 20, 22, 39, 60, 70 and 100 of the murine MN-3 light chain variable region sequence, wherein the antibody or fragment thereof comprises the amino acid sequences of hMN-3VK (SEQ ID NO:18) and hMN-3VH (SEQ ID NO:21), wherein the fragment is selected from the group consisting of Fv, F(ab')2, Fab' and Fab, bound to at least one diagnostic/detection agent or at least one therapeutic agent or is part of a fusion protein, wherein the diagnostic/detection agent comprises a photoactive diagnostic/detection agent, a chromagen or dye, a radionuclide with an energy between 20 and 10,000 keV, a gamma-, beta- or a positron-emitting isotope, a contrast agent, a

paramagnetic ion, an ultrasound-enhancing agent, a liposome or a radiopaque compound, wherein the therapeutic agent is selected from the group consisting of a radionuclide, boron, gadolinium or uranium atoms, an immunomodulator, a cytokine, a hormone, a hormone antagonist, an enzyme, an enzyme inhibitor, a photoactive therapeutic agent, a cytotoxic drug, a toxin, an angiogenesis inhibitor, a different antibody and a combination thereof, wherein the drug is selected from the group consisting of antimitotic, alkylating, antimetabolite, angiogenesis-inhibiting, apoptotic, alkaloid, COX-2-inhibiting and antibiotic agents and combinations thereof, wherein the toxin is selected from the group consisting of ricin, abrin, alpha toxin, saporin, ribonuclease (RNase), DNase I, Staphylococcal enterotoxin-A, pokeweed antiviral protein, gelonin, diphtherin toxin, Pseudomonas exotoxin, and Pseudomonas endotoxin, wherein the immunomodulator is selected from the group consisting of a cytokine, a stem cell growth factor, a lymphotoxin, a hematopoietic factor,: a colony stimulating factor (CSF), an interferon (IFN), a stem cell growth factor, erythropoietin, thrombopoietin, an antibody and a combination thereof.

The claims also recite an antibody fusion protein comprising a first humanized or chimeric antibody or fragment according to claim 1, attached to a second antibody or fragment, wherein the second antibody or fragment is an humanized or chimeric antibody or fragment according to claim 1, wherein the second antibody or fragment binds to an antigen other than NCA90, further comprising a diagnostic/detection or therapeutic agent conjugated to the fusion protein, wherein the second antibody or fragment binds to a granulocyte-associated antigen.

Hansen, et al. teach that an MN-3 antibody was prepared by immunizing mice with a partially purified CEA preparation (page 3479). The instant specification cites the 1993 Hansen, et al. article as the source of the MN-3 antibody (paragraphs 66 and 67). Since the claims recite an MN-3 antibody and the specification discloses the MN-3 antibody to be derived from the Hansen, et al. antibody, the sequence of the instant antibody would be an inherent property of the Hansen, et al. antibody. Hansen, et al. do not teach a chimeric or humanized MN-3 antibody. Hansen, et al. do not teach the antibody conjugated to a therapeutic agent. These deficiencies are made up for in the teachings of Robinson, et al.

Robinson et al (see columns 12-22) teach Fv derived from a known antibody. Robinson et al teach Fv, determination of nucleic acids encoding VH and VL of any known antibody and use of said VH and VL to produce FV (see column 1-45). Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Robinson, et al. teach antibodies of the invention would be advantageously used for development of various immunoconjugates with drugs, toxins, immunomodulators and isotopes (column 38).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody MN-3 and obtain the DNA and protein sequence of the VH and the VL by the method of Robinson, et al. One of ordinary skill in the art would have been motivated to and had a reasonable

expectation of success to have used the antibody MN-3 and obtain the DNA and protein sequence of the VH and the VL by the method of Robinson, et al. because although the references do not teach the amino acid sequences of the MN-3 antibody, Robinson, et al. teach FV, nucleic acids encoding VH and VL and the methods of making FV based on the nucleic acid sequence of any known antibody VH and VL, and methods of determining the nucleic acid sequence of any known antibody VH and VL. All Fv are structurally similar in that they contain similar numbers of amino acids organized in a similar fusion (e.g. they contain a VH and VL wherein the VH and VL contain framework and variable region amino acids). Thus it would not have been undue experimentation to obtain SEQ ID Nos. 1-6, 13, 15, 18, or 21 because the art recognizes that hundreds, if not thousands of antibody molecule VH and VL regions have been cloned and sequenced. Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Thus, the art recognized that there was a reasonable expectation of success that the nucleic acid sequence of the VH and VL of the art known MN-3 antibody could be established using known techniques. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Hansen, et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See

In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The declaration of Hansen filed January 18, 2008 is acknowledged and has been considered by the examiner, however, the declaration does not state that the hybridoma was never given out, only that it was not available "as of the filing date of the instant application of September 30, 2002", which does not fully account for the 9 year time period between 1993 and September 30, 2002.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made as evidenced by the references.

15. Claims 1, 4-6, 8, 9, 14-16, 29, 31, 32, 34-37, 39, and 48-52 are rejected under 35 U.S.C. 103(a) as being obvious over Becker, et al. (Journal of Nuclear Medicine, 1994. Vol. 35, pages 1436-1443, as cited in the previous office action) as evidenced by the specification, in view of Robinson, et al. (US PAT 5,618,920 issued April 1994, as cited in the previous office action).

The claims have been described supra.

Becker, et al. teach a Fab' fragment IMMU-MN3 that specifically binds to NCA-90 available in a kit. Becker, et al. teach labeling of the Fab' fragment with 99m-Tc. Becker, et al. do not teach the sequence of the Fab' fragment or a humanized or chimeric antibody that binds to NCA-90. These deficiencies are made up for in the teachings of Robinson, et al.

Robinson et al (see columns 12-22) teach Fv derived from a known antibody. Robinson et al teach Fv, determination of nucleic acids encoding VH and VL of any known antibody and use of said VH and VL to produce FV (see column 1-45). Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Robinson, et al. teach antibodies of the invention would be advantageously used for development of various immunoconjugates with drugs, toxins, immunomodulators and isotopes (column 38).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the antibody MN-3 and obtain the DNA and protein sequence of the VH and the VL by the method of Robinson, et al. One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the antibody MN-3 and obtain the DNA and protein sequence of the VH and the VL by the method of Robinson, et al. because although the references do not teach the amino acid sequences of the MN-3 antibody, Robinson, et al. teach FV, nucleic acids encoding VH and VL and the methods of making FV based on the nucleic acid sequence of any known antibody VH and VL, and methods of determining the nucleic acid sequence of any known antibody VH and VL. All Fv are structurally similar in that they contain similar numbers of amino acids organized in a similar fusion (e.g. they contain a VH and VL wherein the VH and VL contain framework and variable region amino acids). Thus it would not have been undue experimentation

to obtain SEQ ID Nos. 1-6, 13, 15, 18, or 21 because the art recognizes that hundreds, if not thousands of antibody molecule VH and VL regions have been cloned and sequenced. Robinson et al teach that "The invention also produces consensus sequences and specific oligonucleotide sequences useful as probes for hybridization and priming cDNA synthesis of any hybridoma mRNA coding for variable regions of any desired specificity." (see column 4, last paragraph). Thus, the art recognized that there was a reasonable expectation of success that the nucleic acid sequence of the VH and VL of the art known MN-3 antibody could be established using known techniques. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody of Becker, et al, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

The declaration of Hansen filed January 18, 2008 is acknowledged and has been considered by the examiner, however, the declaration does not state that the hybridoma was never given out, only that it was not available "as of the filing date of the instant application of September 30, 2002", which does not fully account for the 9 year time period between 1993 and September 30, 2002 and Hansen is not an author on the Becker reference.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made as evidenced by the references.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

June 3, 2008

/David J Blanchard/
Primary Examiner, Art Unit 1643